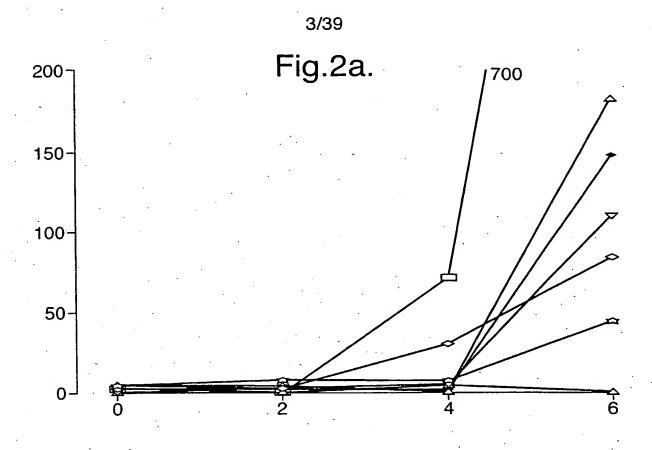
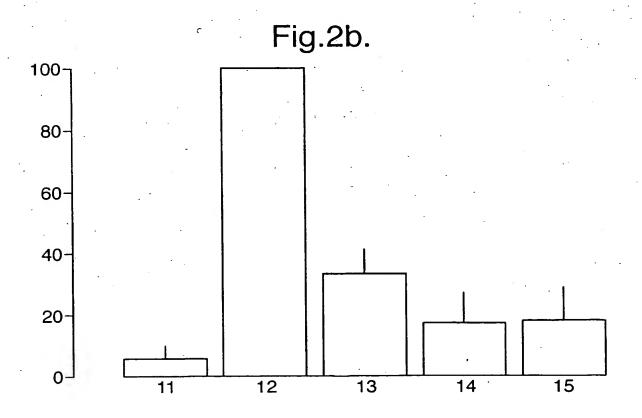


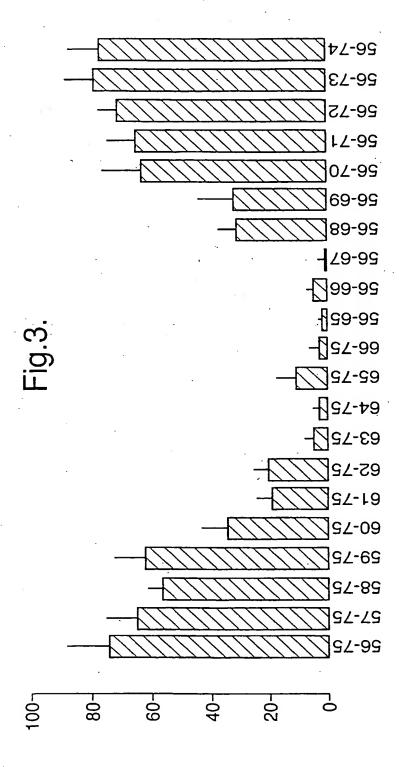
WO 01/25793

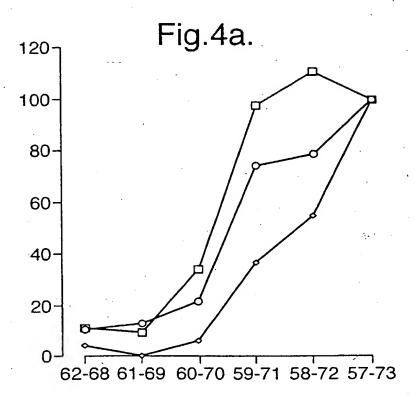
PCT/GB00/03760

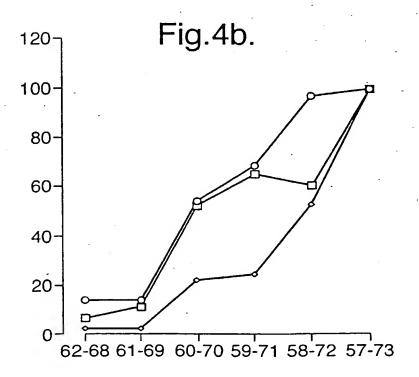


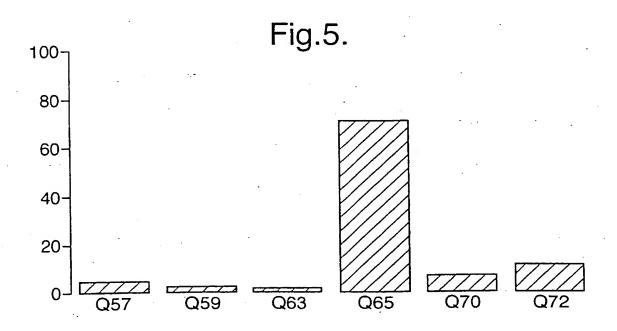


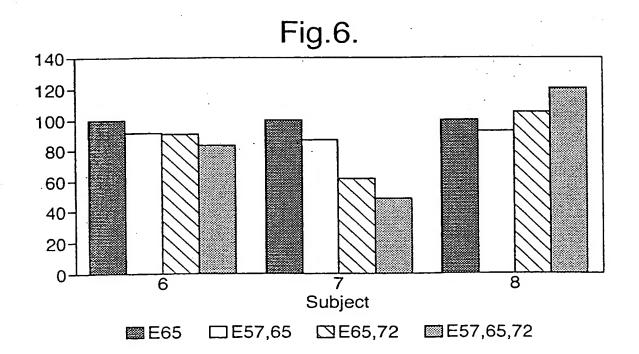
SUBSTITUTE SHEET (RULE 26)

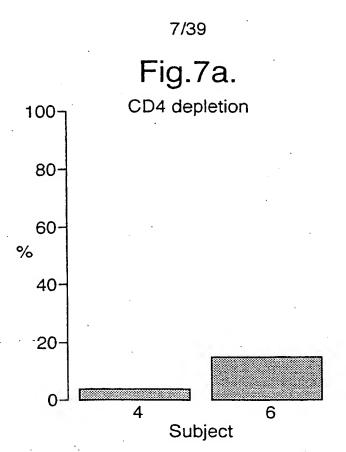


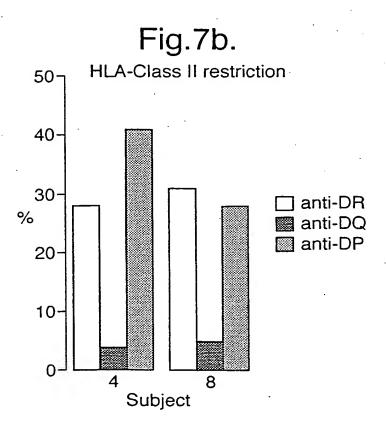




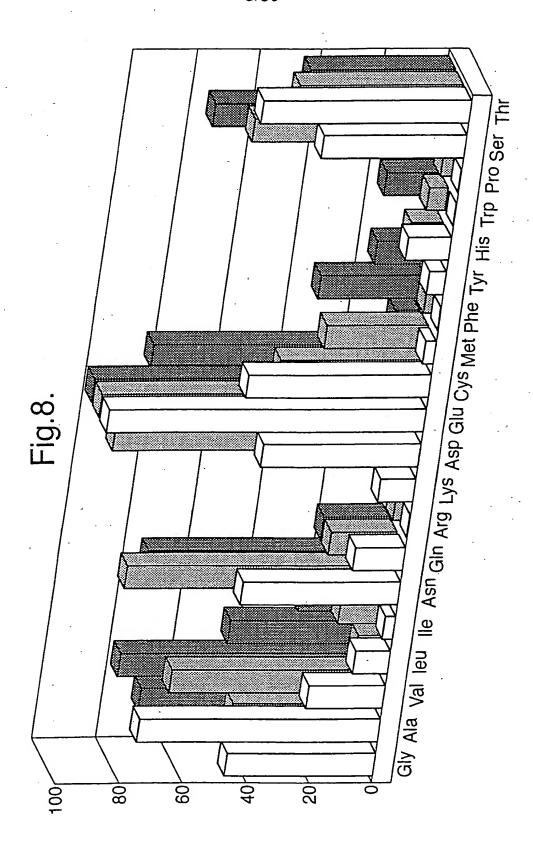




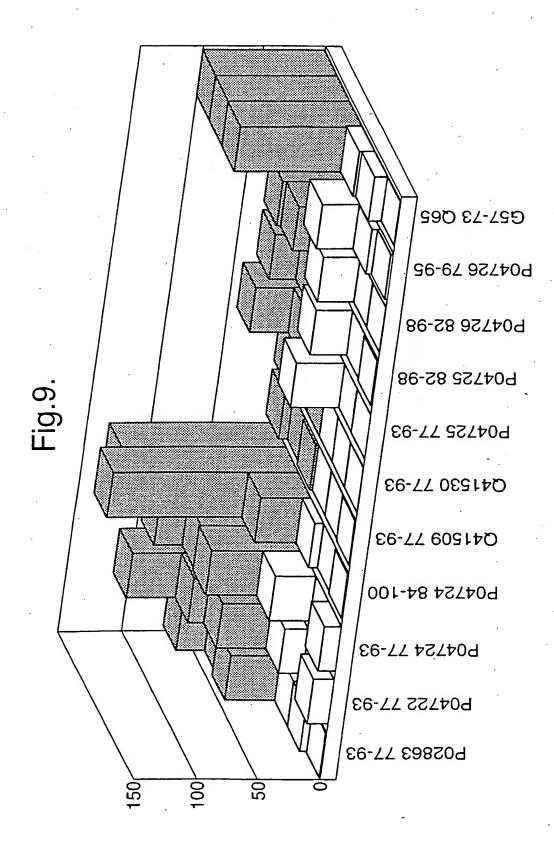


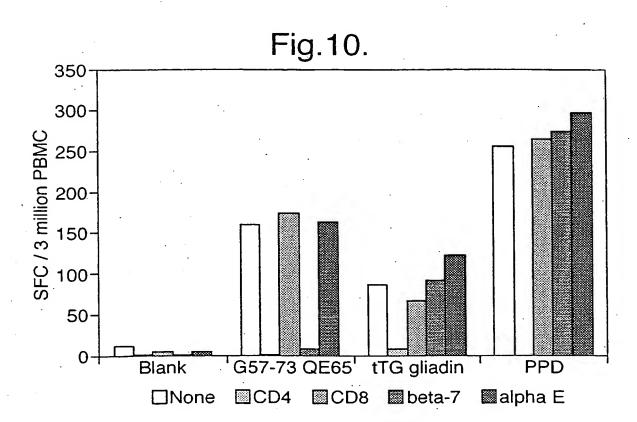


SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)





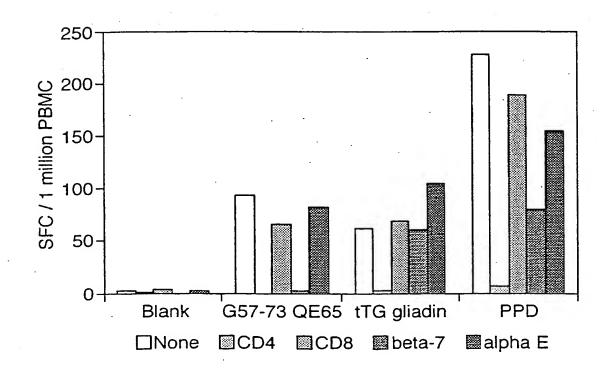


Fig.11.

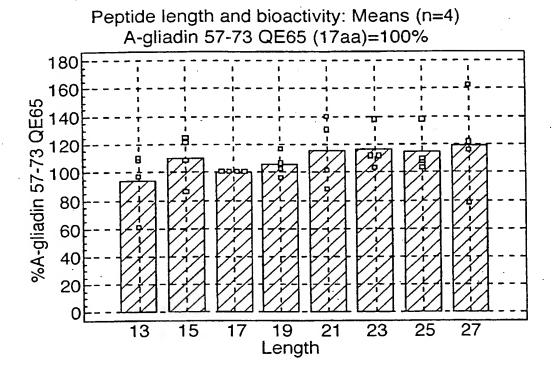


Fig.12a.

Dose response to A-gliadin 57-73 QE65: QLQPFPQPELPYPQPQS.

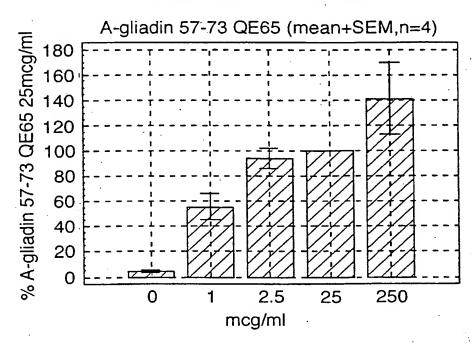
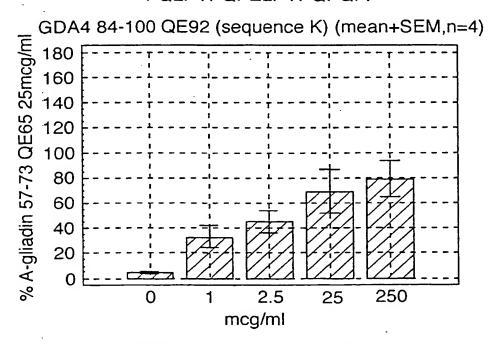


Fig.12b.

Dose response to GDA4_WHEAT P04724 84-100 QE92: PQLPYPQPELPYPQPQP.



SUBSTITUTE SHEET (RULE 26)

Fig.12c.

Dose response to A-gliadin 57-73: QLQPFPQPQLPYPQPQS (2.5, 25 & 250 mcg/ml), and A-gliadin 57-73 (25 mcg/ml) + tTG treatment.

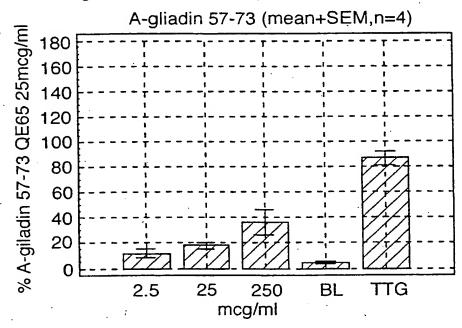
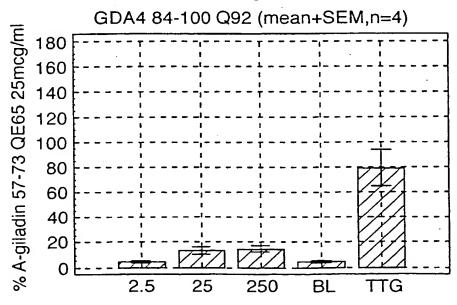


Fig. 12d.

Dose response to GDA4_WHEAT P04724 84-100: PQLPYPQPQLPYPQPQP (2.5, 25 & 250 mcg/ml), and P04724 84-100 (25 mcg/ml) + tTG treatment.



SUBSTITUTE SHEET (RULE 26)

Fig.12e.

Dose response to the DQ2-restricted α gliadin T cell epitope A-gliadin 57-68 QE65: QLQPFPQPELPY (E65) (2.5, 25 & 250 mcg/ml), and A-gliadin 57-68: QLQPFPQPQLPY (Q65) (25 mcg/ml) +/- tTG treatment.

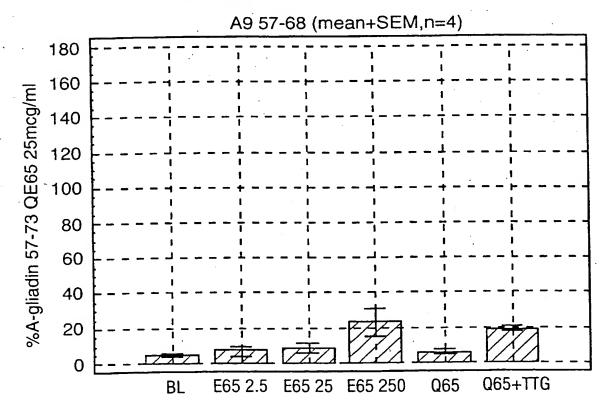
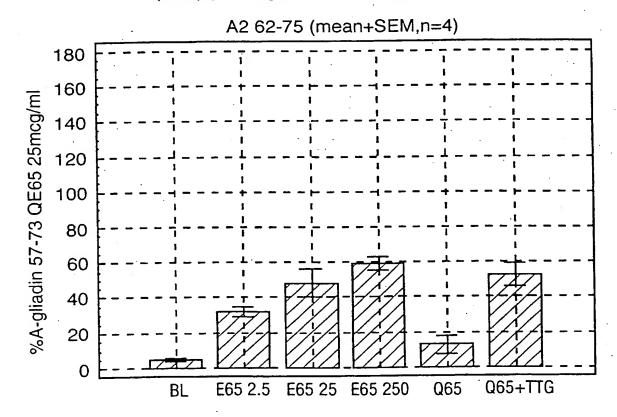


Fig. 12f.

Dose response to the DQ2-restricted α gliadin T cell epitope $\alpha-2$ 62-75 QE65 & QE72: PQPELPYPQPELPY (E65) (2.5, 25 & 250 mcg/ml), and $\alpha-2$ 62-75: PQPQLPYPQPQLPY (Q65) (25 mcg/ml) +/- tTG treatment.

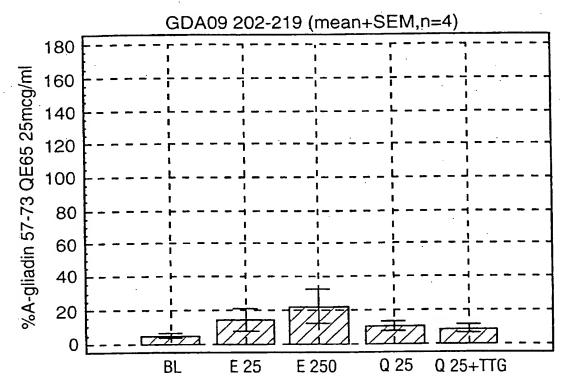


WO 01/25793

16/39

Fig. 12g.

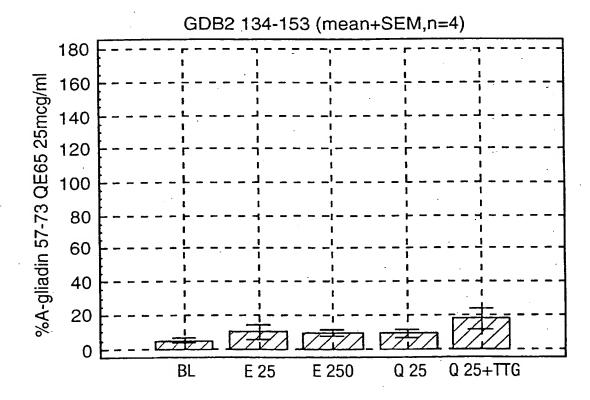
Dose response to the DQ8-restricted α gliadin T cell epitope GDA9 202-219: QE208 & 216: QQYPSGEGSFQPSQENPQ (E) (25 & 250 mcg/ml), and to GDA9 202-219 QQYPSGQGSFQPSQQNPQ (Q) (25 mcg/ml) +/- tTG treatment.



17/39

Fig.12h.

Dose response to the DQ2-restricted γ gliadin T cell epitope GDB2 134-153 QE140, 148,150: QQLPQPEQPQQSFPEQERPF (E) (25 & 250 mcg/ml), and to GDB2 134-153: QQLPQPQQPQQSFPQQQRPF (Q) (25 mcg/ml) +/- tTG treatment.



18/39

Fig.13a.

Dose response to gliadin digest by chymotrysin.

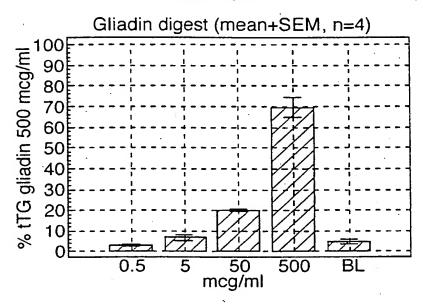


Fig.13b.

Dose response to gliadin digested by chymotrysin then treated with tTG.

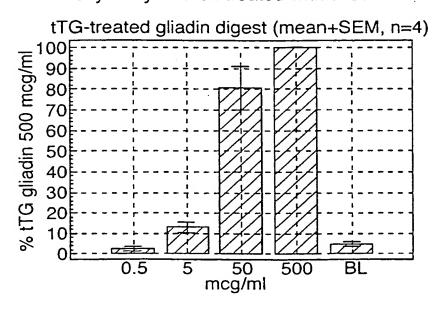
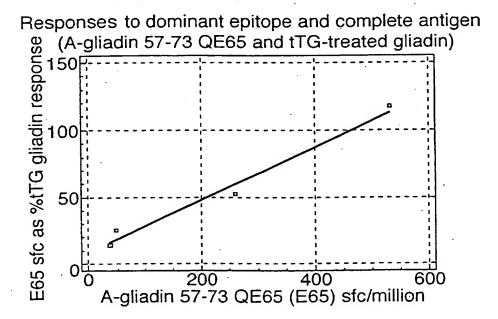
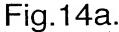


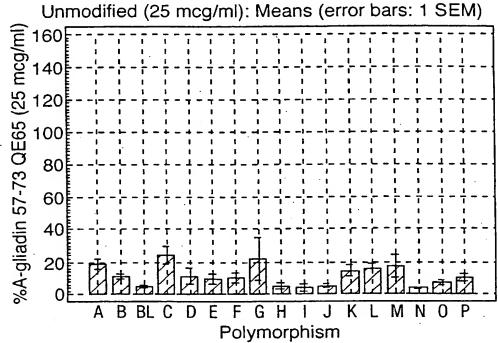
Fig.13c.

Total ELISpot responses to A-gliadin 57-73 QE65 (25mcg/ml) versus A-gliadin 57-73 QE65 responses as percent of tTG gliadin (500mcg/ml) responses.



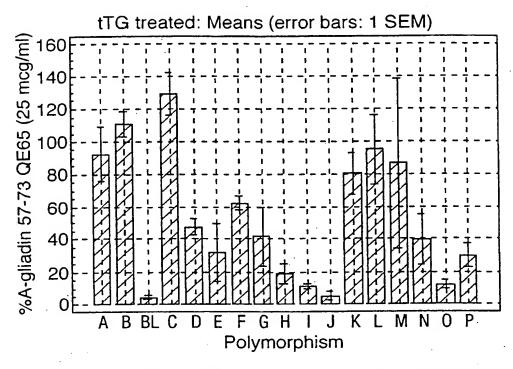
(Fig.14.)
Bioactivity of gliadin polymorphisms of A-gliadin 57-73
(A) in coeliac subjects 6/7 days after gluten challenge
(Gamma-Interferon Elispot) (n=4).





A QLQPFPQP B QLQPFPQP C QLQPFPQP D QLQPFPQP E QLQPFPBP F QLQPFPQP	QLPYPQPQ <u>P</u> QLPYPQPQ <u>L</u> QLPYLQPQS QLPYPQPQP	I J K L M N	QLQPFPQPQLSYSQPQP QPQPFPPPQLPYPQTQP PQLPYPQPQLPYPQPQP PQLPYPQPQLPYPQPQL PQPQPFLPQLPYPQPQS PQPQPFPPQLPYPQPQS
F QLQPFPQP			PQPQPFPPQLPYPQPQS
G QLQPFLQP H QLQPFSQP	QLPYSQPQP	Op	PQPQPFPPQLPYPQTQP PQPQPFPPQLPYPQPPP

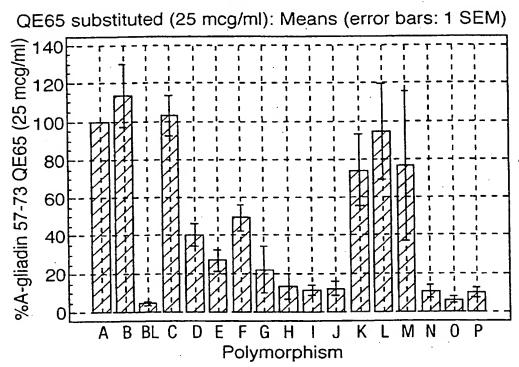
Fig.14b.



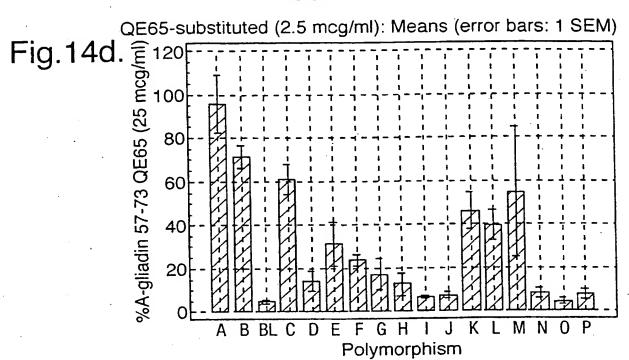
Α	QLQPFPQPQLPYPQPQS
В	QLQPFPQPQLPYPQPQ <u>P</u>
C	QLQPFPQPQLPYPQPQ <u>L</u>
D	QLQPFPQPQLPYLQPQS
E	QLQPFP <u>R</u> PQLPYPQPQP
F	QLQPFPQPQLPY <u>S</u> QPQP
G	QLQPFLQPQLPYSQPQP
Н	QLQPF <u>S</u> QPQLPY <u>S</u> QPQP

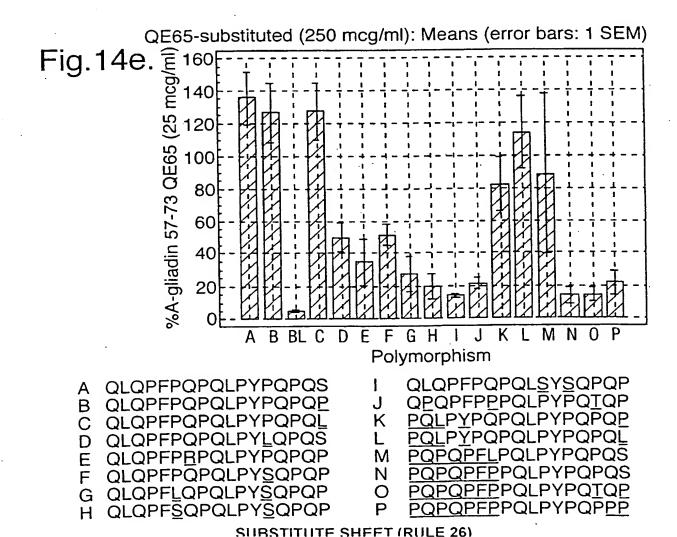


Fig.14c.



Α	QLQPFPQPQLPYPQPQS		QLQPFPQPQLSYSQPQP
В	QLQPFPQPQLPYPQPQ <u>P</u>	J	QPQPFPPPQLPYPQTQP
	QLQPFPQPQLPYPQPQL	K	<u>PQLPYPQPQLPYPQPQP</u>
D	QLQPFPQPQLPYLQPQS	L	PQLPYPQPQLPYPQPQL
Ε	QLQPFPBPQLPYPQPQP	M	PQPQPFL PQLPYPQPQS
	QLQPFPQPQLPYSQPQP	Ν	<u>PQPQPFP</u> PQLPYPQPQS
	QLQPFLQPQLPYSQPQP	0	<u>PQPQPFP</u> PQLPYPQ <u>TQP</u>
	QLQPFSQPQLPYSQPQP	Р	<u>PQPQPFP</u> PQLPYPQP <u>PP</u>

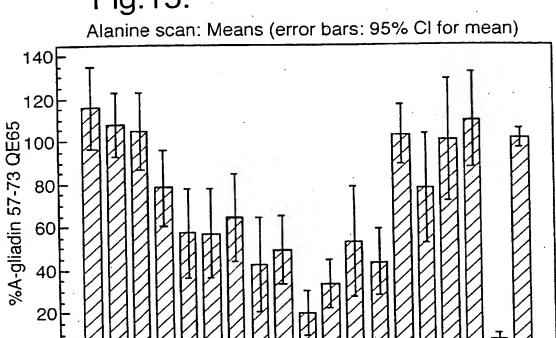




WO 01/25793

Oł.

Fig.15.

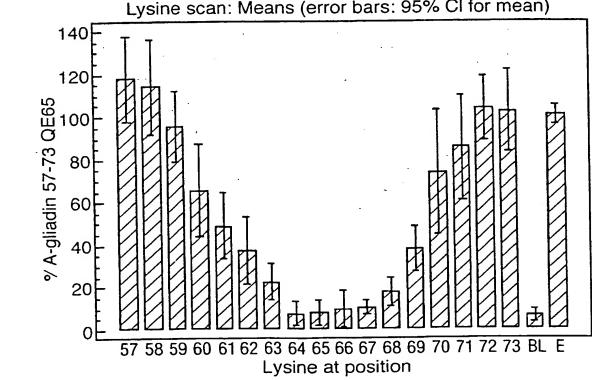


24/39

Fig. 16.

Lysine scan: Means (error bars: 95% Cl for mean)

57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 Alanine at position

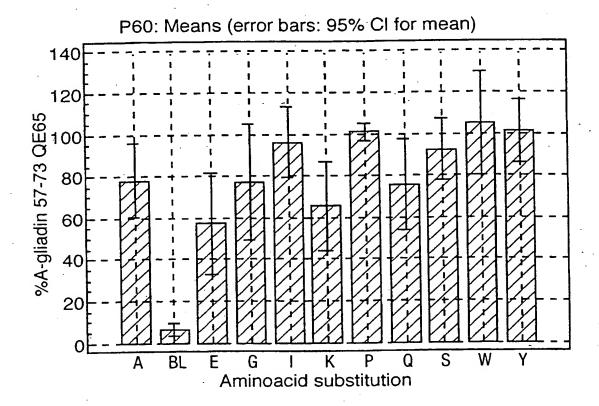


SUBSTITUTE SHEET (RULE 26)

WO 01/25793

25/39

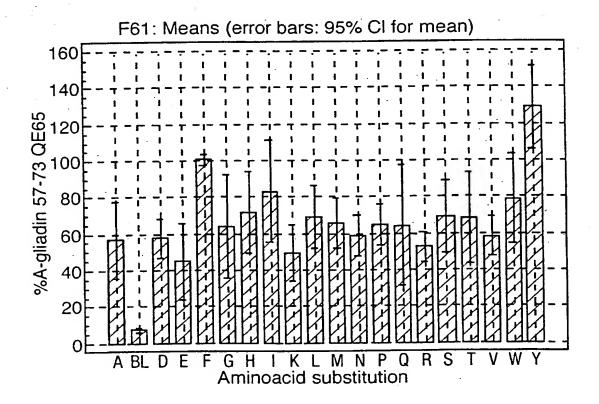
Fig.17.



WO 01/25793

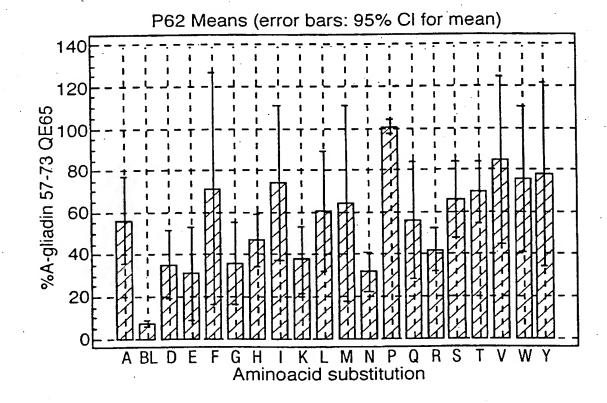
26/39

Fig. 18.



27/39

Fig.19.



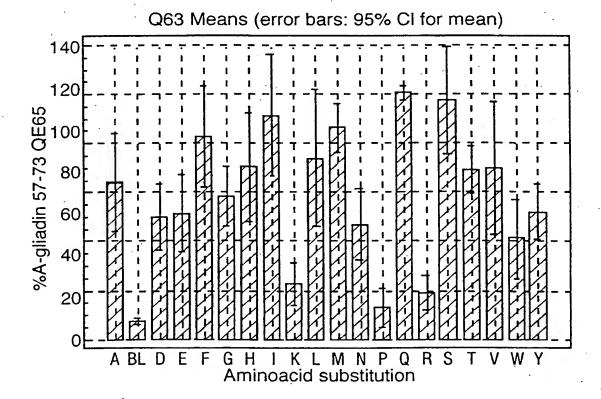
28/39

Fig.20.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

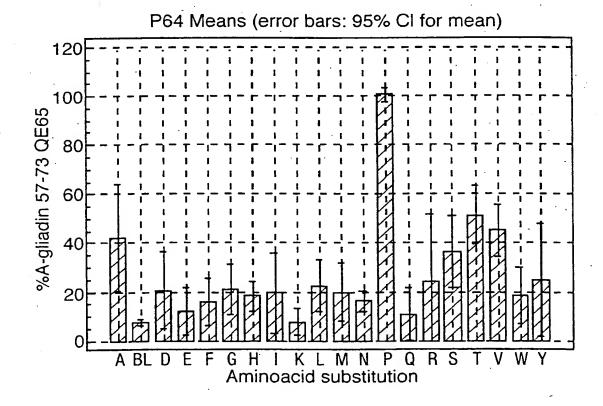
QLQPFPQPELPYPQPQS

60.....70



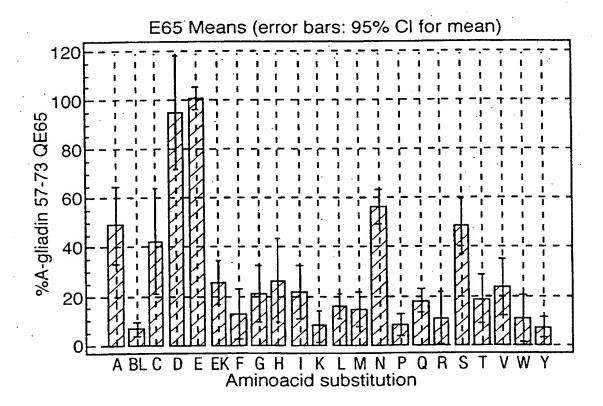
29/39

Fig.21.



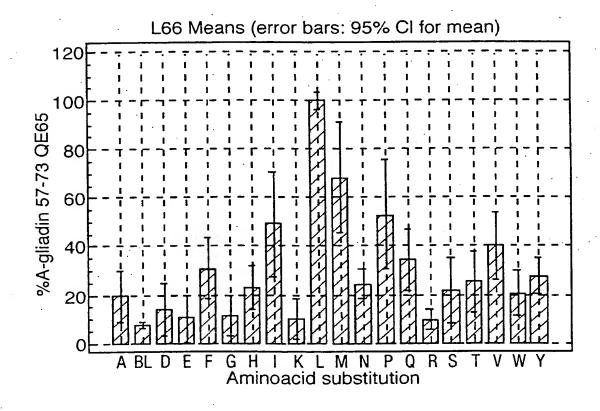
30/39

Fig.22.



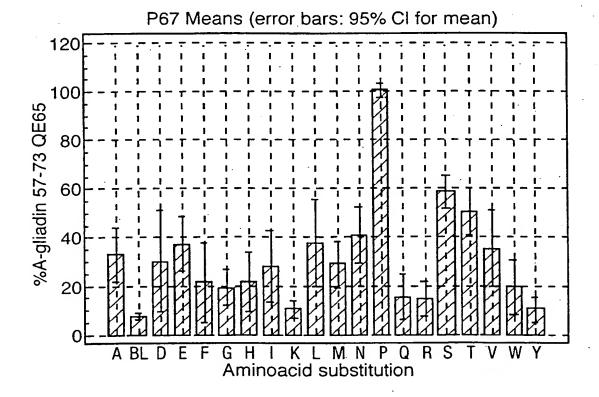
31/39

Fig.23.



32/39

Fig.24.



33/39

Fig.25.

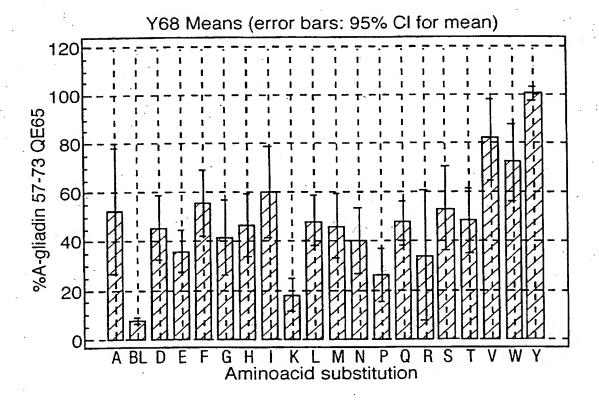


Fig.26.

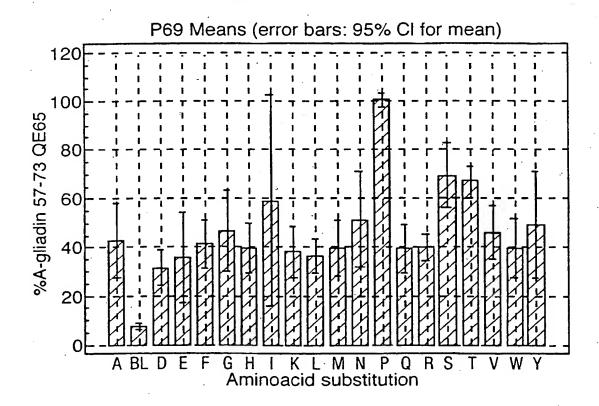
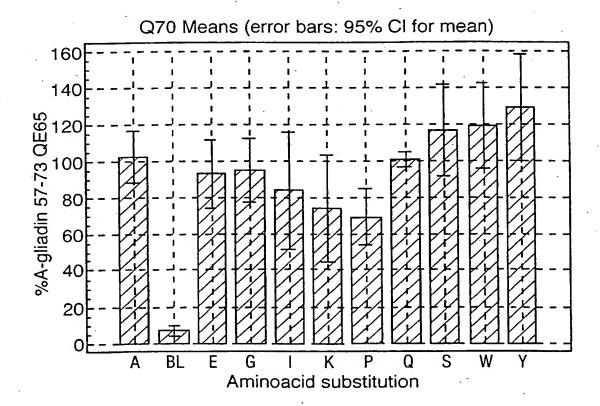


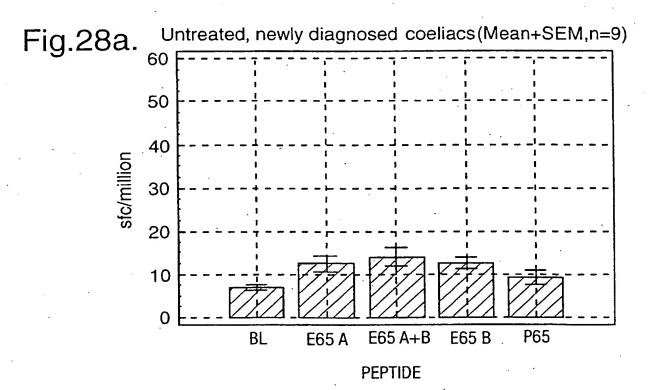
Fig.27.



WO 01/25793

PCT/GB00/03760

(Fig.28.)
Interferon gamma ELISpot responses in newly diagnosed and treated coeliac subjects, before and after gluten challenge.



WO 01/25793

37/39

Fig.28b.

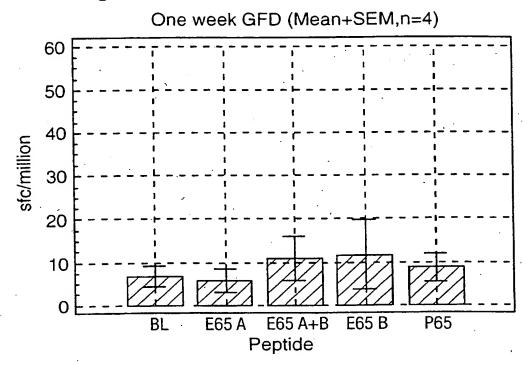
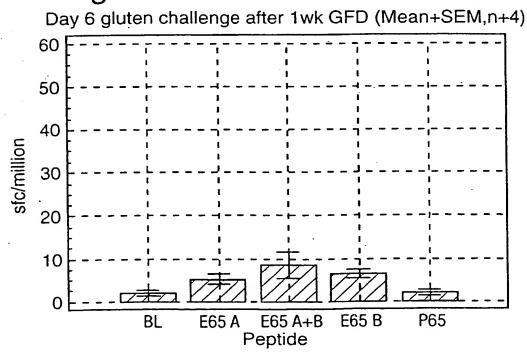


Fig.28c.

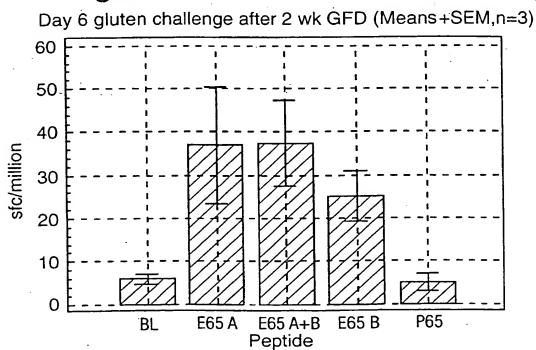


SUBSTITUTE SHEET (RULE 26)

38/39

Fig.28d. Two weeks GFD (Means+SEM,n=3) 60 50 40 sfc/million 30 20 1Ó 0 P65 BL E65 A E65 A+B E65 B Peptide

Fig.28e.



SUBSTITUTE SHEET (RULE 26)

WO 01/25793

39/39

Fig.28f.

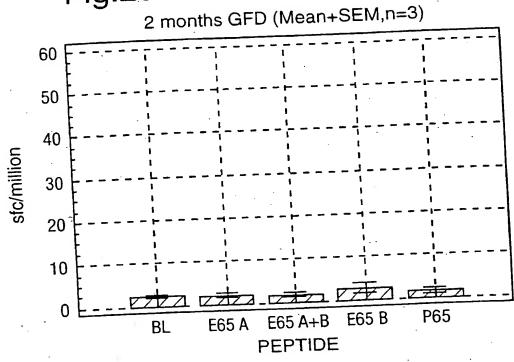
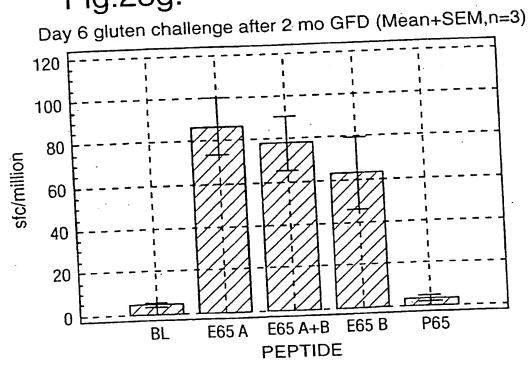


Fig.28g.



CUDETITUTE SHEET (RULE 26)